

IN THE CLAIMS

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the applications.

1. (Currently amended) A method of predicting at least one toxic effect of a compound, comprising:
 - (a) preparing a gene expression profile ~~for~~ a liver tissue or liver cell sample exposed to the compound, said gene expression profile containing the expression level of at least ten genes that are differentially expressed upon exposure to a known hepatotoxin; and
 - (b) comparing the gene expression profile to a database, said database containing mean toxic gene expression values and mean non-toxic gene expression values for said at least ten genes, said mean toxic gene expression values being generated from hepatocytes exposed to said known hepatotoxin comprising at least part of the data or information of Tables 1-5.
2. (Canceled)
3. (Currently amended) ~~The~~A method of claim 12, wherein said at least ten genes correspond to sequences listed in one of Tables 5A-5W~~WW~~the level of expression is compared to a Tox-Mean and/or Non-Tox-Mean value in Tables 1-5.
4. (Currently amended) ~~The~~A method of claim 3, wherein the gene expression levels of said at least ten genes are~~the level of expression is~~ normalized prior to comparison.
5. (Currently amended) ~~The~~A method of claim 4, wherein the database comprises substantially all of the data or information in Tables 1-5.
6. (Canceled)

7. (Currently amended) A method of predicting at least one toxic effect of a compound, comprising:

(a) detecting the level of expression in a tissue or cell sample exposed to the compound of two or more genes corresponding to sequences from one of Tables 5B, 5H, 5J, 5P, 5R, 5Y, 5AA, 5CC, 5EE, 5KK, 5OO, 5QQ, 5YY, 5AAA, 5CCC, 5JJJ, 5QQQ, and 5WWW; wherein differential expression of ~~said~~the genes in Tables 5B, 5H, 5J, 5P, 5R, 5Y, 5AA, 5CC, 5EE, 5KK, 5OO, 5QQ, 5YY, 5AAA, 5CCC, 5JJJ, 5QQQ, and 5WWW is indicative of the at least one toxic effect.

8. (Currently amended) A method of predicting the progression of a toxic effect of a compound, comprising:

(a) detecting the level of expression in a tissue or cell sample exposed to the compound of two or more genes corresponding to sequences from one of Tables 5B, 5H, 5J, 5P, 5R, 5Y, 5AA, 5CC, 5EE, 5KK, 5OO, 5QQ, 5YY, 5AAA, 5CCC, 5JJJ, 5QQQ, and 5WWW, wherein differential expression of ~~said~~the genes in Tables 5B, 5H, 5J, 5P, 5R, 5Y, 5AA, 5CC, 5EE, 5KK, 5OO, 5QQ, 5YY, 5AAA, 5CCC, 5JJJ, 5QQQ, and 5WWW is indicative of toxicity progression.

9. (Currently amended) A method of predicting the hepatotoxicity of a compound, comprising:

(a) detecting the level of expression in a liver tissue or liver cell sample exposed to the compound of two or more genes corresponding to sequences from one of Tables 5B, 5H, 5J, 5P, 5R, 5Y, 5AA, 5CC, 5EE, 5KK, 5OO, 5QQ, 5YY, 5AAA, 5CCC, 5JJJ, 5QQQ, and 5WWW, wherein differential expression of ~~said~~the genes in Tables 5B, 5H, 5J, 5P, 5R, 5Y, 5AA, 5CC, 5EE, 5KK, 5OO, 5QQ, 5YY, 5AAA, 5CCC, 5JJJ, 5QQQ, and 5WWW is indicative of the hepatotoxicity.

10. (Currently amended) A method of identifying an agent that modulates the onset or progression of a toxic response, comprising:

- (a) exposing a cell to the agent and a known toxin; and
- (b) detecting the expression level in said cell of two or more genes corresponding to sequences from one of Tables 5B, 5H, 5J, 5P, 5R, 5Y, 5AA, 5CC, 5EE, 5KK, 5OO, 5QQ, 5YY, 5AAA, 5CCC, 5JJJ, 5QQQ, and 5WWW; wherein differential expression of saidthe genes-in Tables 1-3 is indicative of the toxic responsetoxicity.

11. (Canceled)

12. (Previously Presented) The method of claim 7, wherein the expression levels of at least 3 genes are detected.

13. (Previously Presented) The method of claim 7, wherein the expression levels of at least 4 genes are detected.

14. (Previously Presented) The method of claim 7, wherein the expression levels of at least 5 genes are detected.

15. (Previously Presented) The method of claim 7, wherein the expression levels of at least 6 genes are detected.

16. (Previously Presented) The method of claim 7, wherein the expression levels of at least 7 genes are detected.

17. (Previously Presented) The method of claim 7, wherein the expression levels of at least 8 genes are detected.

18-19. (Canceled)

20. (Currently amended) TheA method of claim 7, wherein the effect is selected from the group consisting of carcinogenesis, cholestasis, hepatitis, liver enlargement, inflammation, liver necrosis, liver steatosis and peroxisome proliferation.

21. (Currently amended) TheA method of claim 9, wherein the hepatotoxicity is associated with at least one liver disease pathology selected from the group consisting of carcinogenesis, cholestasis, hepatitis, liver enlargement, inflammation, liver necrosis, liver steatosis and peroxisome proliferation.

22. (Currently amended) TheA method of claim 144, wherein the toxic effect is the effect produced by cellular pathway is modulated by a toxin selected from the group consisting of acetaminophen, 2-acetylaminofluorene (2-AAF), acyclovir, ANIT, AY-25329, BI liver toxin, chloroform, bicalutamide, carbon tetrachloride, chloroform, CI-1000, clofibrate, colchicine, CPA, diclofenac, diflunisal, dimethylnitrosamine (DMN), dioxin, 17 α -ethinylestradiol, gemfibrozil, hydrazine, indomethacin, LPS, menadione, phenobarbital, tacrine, thioacetamide, valproate, Wy-14643 and zileuton.

23-45. (Canceled)

46. (Currently amended) TheA method of claim 10, wherein the known toxin is a hepatotoxin.

47. (Currently amended) TheA method of claim 143, wherein the known hepatotoxin is selected from the group consisting of acetaminophen, 2-acetylaminofluorene (2-AAF), acyclovir, ANIT, AY-25329, BI liver toxin, chloroform, bicalutamide, carbon tetrachloride, chloroform, CI-1000, clofibrate, colchicine, CPA, diclofenac, diflunisal, dimethylnitrosamine (DMN), dioxin, 17 α -ethinylestradiol, gemfibrozil, hydrazine, indomethacin, LPS, menadione, phenobarbital, tacrine, thioacetamide, valproate, Wy-14643 and zileuton.

48. (Currently amended) TheA method of claim 7, wherein ~~neary~~ expression of all of the genes corresponding to all of the sequences in Tables 5B, 5H, 5J, 5P, 5R, 5Y, 5AA, 5CC, 5EE, 5KK, 5OO, 5QQ, 5YY, 5AAA, 5CCC, 5JJJ, 5QQQ, and 5WWW are detected.

49. (Currently amended) TheA method of claim ~~7~~48, wherein ~~expression all of the genes~~ corresponding to all of the sequences in at least one of Tables 5B, 5H, 5J, 5P, 5R, 5Y, 5AA, 5CC, 5EE, 5KK, 5OO, 5QQ, 5YY, 5AAA, 5CCC, 5JJJ, 5QQQ, and 5WWW are detected.

50-52. (Canceled)

53. (Currently amended) TheA method of claim 7, wherein the compound exposure is *in vivo* or *in vitro*.

54. (Currently amended) TheA method of claim 7, wherein the level of expression is detected by an amplification or hybridization assay.

55. (Currently amended) TheA method of claim 54, wherein the amplification assay is quantitative or semi-quantitative PCR.

56. (Currently amended) TheA method of claim 54, wherein the hybridization assay is selected from the group consisting of Northern blot, dot or slot blot, nuclease protection and microarray assays.

57. (Canceled)

61. (Currently amended) TheA method of claim ~~34~~31, wherein the mean toxic gene expression values and/or the mean non-toxic gene expression values are listed~~level of expression is compared to a Tox Mean and/or Non-Tox Mean value in one of~~ Tables 5A-5WWW.

62-65. (Canceled)

66. (New) The method of claim 1, wherein the toxic effect is at least one of carcinogenesis, cholestasis, hepatitis, liver enlargement, inflammation, liver necrosis, liver steatosis, and peroxisome proliferation.

67. (New) The method of claim 8, wherein the toxic effect is at least one of carcinogenesis, cholestasis, hepatitis, liver enlargement, inflammation, liver necrosis, liver steatosis, and peroxisome proliferation.

68. (New) The method of claim 10, wherein the toxic response is at least one of carcinogenesis, cholestasis, hepatitis, liver enlargement, inflammation, liver necrosis, liver steatosis, and peroxisome proliferation.

69. (New) The method of claim 10, wherein the known toxin is acetaminophen, 2-acetylaminofluorene (2-AAF), acyclovir, ANIT, AY-25329, BI liver toxin, chloroform, bicalutamide, carbon tetrachloride, chloroform, CI-1000, clofibrate, colchicine, CPA, diclofenac, diflunisal, dimethylnitrosamine (DMN), dioxin, 17 α -ethinylestradiol, gemfibrozil, hydrazine, indomethacin, LPS, menadione, phenobarbital, tacrine, thioacetamide, valproate, Wy-14643 or zileuton.